

and an adjacent region of about 30 residues containing a heptad repeat of leucines, the "leucine zipper" (5) [5. W.H. Landschultz, P.B. Sigler, S.L. McKnight, *ibid.* 240, 911 (1989)], that mediates dimerization. Such bZIP dimers bind DNA sites that are approximately diad-symmetric (3) [Reviewed by P.F. Johnson and S.L. McKnight, *Annu. Rev. Biochem.* 58, 799 (1989); K. Struhl, *Trends Biochem. Sci.* 14, 137 (1989)].

and later:

b2
A peptide (GCN4-brl), corresponding to residues 222 to 252 of GCN4 (22) [22. G. Thireos, M.D. Penn, H. Greer, *Proc. Natl. Acad. Sci. U.S.A.*, 81, 5097 (1984); A.G. Hinnebusch, *ibid.*, p. 6442.], was synthesized (23) [Peptides were synthesized on an Applied biosystems Model 430A peptide synthesizer with standard reaction cycles modified to include acetic anhydride capping. Peptides were cleaved from the resins by low-high HF cleavage (Immunodynamics, Inc., San Diego, CA) and desalted by Sephadex G-10 chromatography in 5% acetic acid. Purifications were by high-performance liquid chromatography with a Vydac reverse-phase C₁₈ column and a linear gradient of CH₃CN-H₂O with 0.1% trifluoroacetic acid. Fast atom bombardment mass spectrometry; GCN4-brl: calculated, 3796.5; found, 3795.8; GCN4-bZIP1: calculated, 7015.4 found, 7015.5.] with a Gly-Gly-Cys linker (6) [6. E.K. O'Shea, R. Rutkowski, P.S. Kim, *ibid.* 243, 538 (1989)] added at the carboxyl terminus (Fig. 1). The glycines were included to provide a flexible linker in the disulfide-bonded dimer, referred to as GCN4-brl^{ss}". The peptide was made as the carboxyl-terminal amide to avoid introduction of additional charge. A second peptide (GCN4-bZIP1), corresponding to the entire bZIP region of GCN4 (residues 222 to 281), was also synthesized (Fig. 1). This 60-residue peptide is capable of dimerization and sequence-specific DNA binding (8) [8. I.A. Hope and K. Struhl, *Cell* 46, 885 (1986)].

Figure 1 at 769 states:

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Sequences of the peptides studied (23) [23. Peptides were synthesized on an Applied biosystems Model 430A peptide synthesizer with standard reaction cycles modified to include acetic anhydride capping. Peptides were cleaved from the resins by low-high HF cleavage (Immunodynamics, Inc., San Diego, CA) and desalted by Sephadex G-10 chromatography in 5% acetic acid. Purifications were by high-performance liquid chromatography with a Vydac reverse-phase C₁₈ column and a linear gradient of CH₃CN-H₂O with 0.1% trifluoroacetic acid. Fast atom bombardment mass spectrometry; GCN4-brl: calculated, 3796.5; found, 3795.8; GCN4-bZIP1: calculated, 7015.4 found, 7015.5.]. GCN4-bZIP1 consists of the 60 carboxyl-terminal residues of GCN4 (22). The leucines in the leucine repeat are underlined. GCN4-brl consists of the basic region residues (boxed) plus the carboxyl-terminal linker Gly-Gly-Cys. Abbreviations for the amino acid residues are: A, Ala; C, Cys; D, Asp; E, Glu; G, Gly; H, His; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; and Y, Tyr.

Page 15, line 17, after "566]", insert /--Ashley, et al. state in Figure 1 at 563:

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Location and homologies of RNP family domains in FMRP. [Fig. 14] (A) Alignment (27) [27. M. Gribskov, R. Leuthy, D. Eisenberg, *Methods Enzymol.* 183, 146 (1989)]. The 12-residue element is not found in the sequence of *Drosophila* HSF. It is possible that another element may serve the same function.] of the amino acid sequences that make up the KH domains of FMRP and several other proteins and the corresponding consensus sequence. Numbers in parentheses indicate the particular domain shown for the proteins that have multiple KH domains, and the number preceding the first residue indicates that position in the corresponding protein. Dark highlighting indicates similarities among all proteins, whereas stippled highlighting indicates similarity between the two KH domains of FMRP. Boldface residues show the

positions of polar amino acids, indicated by f in the consensus sequence. The bracketed lysine (K) residues indicate this amino acid at either position in the domain. The position of the isoleucine-to-asparagine mutation at position 304 (I³⁰⁴ → N) in a patient (6) [D. Wohrle, et al., *Am. J. Hum. Genet.* 51, 299 (1992); A.K. Gideon, et al., *Nature Genet.* 1, 341 (1992); K. De Boulle et al., *ibid.* 3, 31 (1993)] is indicated at the bottom. [Fig. 15] [1. W.T. Brown, *Am. J. Hum. Genet.* 47, 175 (1990); S.L. Sherman et al., *Ann. Hum. Genet.* 48, 21 (1984); 2. M.G. Butler, T. Mangrum, R. Gupta, D.N. Singh, *Clin. Genet.* 39, 347 (1991); 3. A.M. J.G. Verkerk, et al., *Cell* 65, 905 (1991); I. Oberle et al., *Science* 252, 1097 (1991); E.J. Kremer et al., *ibid.* p. 1711; A. Vincent et al., *Nature* 349, 624 (1991)]. (B) Diagram of FMRP [residue numbers are as described (7)]. [7. C.T. Ashley et al., *Nature Genet.* 4, 244 (1993)] The CGG repeat and initiating codon (M¹) are indicated as is each KH domain, labeled 1 and 2. Also shown is the amino acid sequence with the two RGG box domains highlighted. Abbreviations for the amino acid residues are: A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.

Figure 1 a and b are reproduced as Figures 14 and 15.

Page 15, line 19, after "(1993)]", insert /--Rabitindran, et al., state in Figure 1 at 231:

Fig. 1. [Fig. 16] Activity of wild-type and mutant human HSF1 proteins transiently expressed in 293 cells. Map of wild-type and mutant human HSF1 (hHSF) ORFs is at left. Numbers on the right indicate the end point of the truncated fragments; amino acids in the fourth hydrophobic repeat and appended by cloning at the COOH-terminal and are represented by the single-letter code (30). [30. Abbreviations for the amino acid residues are as follows: A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q,